

# TRACT-BASED QUANTITATIVE ANALYSIS OF MYELIN AND AXONAL REMODELING IN THE UNINJURED MOTOR NETWORK AFTER STROKE

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**Introduction.** Previous works from our group showed axonal and myelin plasticity in the uninjured motor network of stroke patients with motor deficits [1-2]. However, these studies focused on average MRI indexes of tract integrity namely generalized fractional anisotropy (GFA) [3] for axonal properties and magnetization transfer ratio (MTR) [4] for myelin characteristics. These approaches offered a global view of tract remodeling but failed in revealing subtle changes affecting only partially single motor connections. Depending on the location and extension of the stroke lesion, in fact, parts of connections might be more susceptible than other to plastic changes over time. In this study, we performed track-based quantitative analysis for assessing GFA and MTR values along the tract and characterizing their variations at large- and small-scale.

**Methods.** Ten patients (Age: 56.1±17.8; female:male=4:6) underwent 3 DSI and 3 MT scans, in the acute phase (within 1 week after the stroke onset, tp1), 1 month (±1 week, tp2) and 6 months (±15 days, tp3) after stroke, respectively. Patients benefitted of clinical assessment (NIHSS, FIM and RANKIN scores)

at each time point. Ten healthy controls, HC (Age: 60.3±12.8; female:male=4:6) benefitted of DSI and MT scans twice within a 1 month interval (±1 week, tp1c and tp2c). DSI scans were performed as follow: TR/TE=6600/138 ms, FoV=212x212 mm, 34 slices, 2.2x2.2x3 mm<sup>3</sup> resolution, 257 diffusion directions, b<sub>max</sub>=8000 s/mm<sup>2</sup> [1]. MT scans were performed using a multiple-echo Fast Low Angle SHot (FLASH) sequence with (MT) and without (M0) magnetization transfer preparation (TR/TE = 48/23 ms, FoV = 240x256x96, 2x2x2 mm<sup>3</sup> resolution, 8 echoes). Reconstruction of the motor network was performed as in [1]. All measurements were performed at 3T (Trio a Tim System, Siemens, Erlangen, Germany) using a 32-channel head coil.

The following brain regions, and their corresponding connectivity, were considered: primary motor area (M1), secondary motor areas (SMA, PMv and PMd). The connections between motor areas in the same hemisphere were labeled as intra-hemispheric and the ones between motor areas and the corpus callosum (CC) were considered as inter-hemispheric. Magnetization transfer ratio was calculated as  $MTR=(M0-MT)/M0*100$  and GFA was obtained as in [3]. Tract-based GFA and MTR histograms were obtained and the following density derived features were calculated: mean, peak height, standard deviation (SD) and skewness (figure 1C). In figure 1C, each node of graph corresponds to the motor cortical areas, and each edge to the significance value estimating the difference across groups for each connection. A t-test followed by multi-group comparison with False Discovery Rate (FDR) [5] was used to determine the significance of the observed differences across groups (i.e. tp1-2 patients vs. tp1-2 HC).

**Results.** Changes in MTR values along the intra-hemispheric motor connections were significantly different between patients and healthy controls within one month after stroke, figure 2A (tp1-2-tp1-2 HC): reduced peak height was in fact observed in M1-SMA, M1-PMd, PMd-PMv, p < 0.05 corrected, increased SD in M1-SMA and PMd-PMv, p < 0.05 corrected and increased skewness in M1-SMA, p < 0.05 corrected. Density-derived features (peak height, SD and skewness) appeared more sensitive than the mean to describe myelination changes in motor connections. Only changes in GFA along intra-hemispheric M1-SMA were significantly different between patients and HC within one month after stroke, figure 2B (tp1-2-tp1-2 HC): increased skewness was in fact observed in M1-SMA, p < 0.05 corrected). Also, no statistically significant dependence was observed between MTR and GFA changes.

## Longitudinal Graph Pipeline

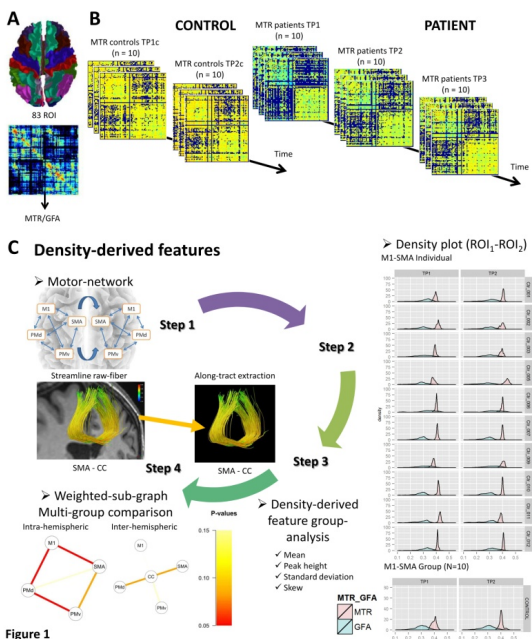


Figure 1

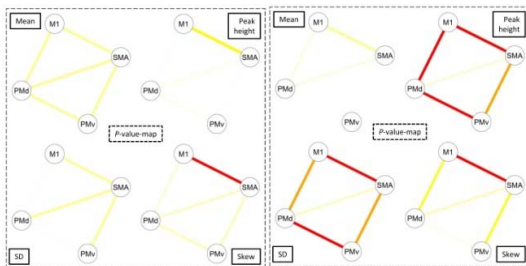


Figure 2B

Figure 2A

**Discussion and Conclusion** Tract-based analysis of MTR and GFA changes in the uninjured motor network after stroke showed significant changes in a number of motor connections, confirming both axonal and myelin plasticity. Histograms density-derived features appear more sensitive than mean changes to detect connectivity remodeling after stroke. Future work should assess the value of those parameters in predicting clinical outcome after stroke.

**References.** [1] Granziera C. et al. , *Neurology*, 2012. [2] Lin Y.C. et al. , *ISMRM*, 2013. [3] Tuch DS. , *Magn Reson Med*, 2004. [4] Beaulieu, C. *NMR Biomed*, 2002. [5] Benjamini Y. et al. , *Journal of the Royal Statistical Society Series B (Methodological)*, 1995.